

## REMARKS

### I. Status of Claims

Claims 1-4, 7-11, 13-15, 20, and 25 are pending.

### II. Objection to the Specification

The disclosure was objected to since trademarks should be capitalized and be accompanied by generic terminology.

#### Response

Trademarks have been amended to be capitalized and generic terminology thereto has been added. Applicants believes this amendment obviates this objection to the specification and request that the objection be withdrawn.

### III. Ownership of Claimed Invention

The subject matter of the claims was commonly owned at the time the claimed invention was made.

### IV. Rejection of Claims under §103(a)

Claims 1-4, 7-11, 13-15, 20, and 25 were rejected as unpatentable over Ram *et al.* Compound #17 of Table 1 on page 541 of Ram was cited as reading on the claimed generic compound. Compound #17 has a fluorine on a benzyl ring. The Office Action states that the compound has antineoplastic activity and that modification of the compound to substitute the fluorine with a hydrogen would have been obvious because such a substitution would not be expected to materially alter the antineoplastic activity of the compound.

#### Response

Applicants point out that Table 1 of Ram has no data for compound #17 for antineoplastic activity. The information in column three of Table 1 states "No data. Sol. too low." The data of the last three columns are for antifilarial activity against the filarial worm *B. pahangi*. Such antifilarial activity does not teach or suggest antineoplastic activity.

Benzimidazole 3-7 of Table 3 of the specification has formula A-3 where R<sub>1</sub> is unsubstituted benzyl. The data of Table 4 state that the IC<sub>50</sub> (μM) for compound 3-7 is 0.085 for murine melanoma and 0.033 for human colon carcinoma.

The Federal Circuit has required that specific support must be found in the prior art that "suggests" or "teaches" the modification necessary to resolve the differences of the prior art with a

claimed invention. *In re Grabiak*, 226 USPQ 870 (Fed. Cir. 1985). Applicants submit that no such support for making the structural and chemical changes to compound #17 of *Ram et al.* necessary to resolve the differences with the claimed invention is present in *Ram, et al.*

Since *Ram et al.* do not render the compound claims obvious, *Ram et al.* cannot render claims to compositions relating to the compound obvious. Applicants respectfully request that this rejection be withdrawn.

#### V. Conclusion

It is believed that all matters of the Office Action have been addressed. Reconsideration and an early indication of the allowability of the claims are earnestly requested. Should the Examiner have any questions, comments or suggestions that would expedite the prosecution of the present case to allowance, Applicants' undersigned representative earnestly requests a telephone conference at (512) 867-8528.

Respectfully submitted,

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**ATTACHMENT A**  
**VERSION WITH MARKINGS TO SHOW CHANGES MADE**  
(language to be added is underlined and language to be deleted is enclosed in brackets)

**In the Specification**

At page 16, the paragraph beginning at line 25 is amended as indicated below:

DNA topoisomerase II inhibitors include the following intercalators, such as amsacrine, dactinomycin, daunorubicin, doxorubicin ([adriamycin] ADRIAMYCIN®), idarubicin, and mitoxantrone; nonintercalators, such as etoposide and teniposide, for example.

At page 17, the paragraph beginning at line 28 is amended as indicated below:

[Taxol] TAXOL® (paclitaxel) is a preferred chemotherapeutic agent.

At page 22, the paragraph beginning at line 13 is amended as indicated below:

Further potentiators include, but are not limited to, propionic acid, salts thereof, or esters thereof; antioxidant vitamins such as vitamins A, C, E, or beta-carotene; abacavir; AL-721 (lipid mixture); amprenavir; Amphotericin B methyl ester; [Ampligen] AMPLIGEN® (mismatched RNA); anti-AIDS antibody; anti-human interferon- $\alpha$  antibody; anti-AIDS antibody, ascorbic acid and derivatives thereof; AS-101 (heavy metal based immunostimulant); azidothymidine;  $\beta$ -interferon; Bropirimine; butylated hydroxytoluene; Ciamexon, Cimetidine; CL-246,738, colony stimulating factors, including GM-CSF; Creme Pharmatex (benzalkonium chloride); CS-82 (5-unsubstituted derivative of Zidovudine); Cyclosporin; D-penicillamine (3-mercapto-D-valine); delavirdine; dextran sulphate; dinitrochlorobenzene; efavirenz; erythropoietin; Foscarnet (trisodium phosphonoformate); fusidic acid; ganciclovir; glucan; glycyrrhizin, HPA-23 (ammonium-21-tungsto-9-antimonate); human immunovirus antiviral; hyperimmune gamma-globulin, IMREG®-1, IMREG®-2 (small molecular weight substances extracted from the white blood cells of humans, used to treat disorders of the human immune system); indinavir; interferon- $\alpha$ ; interferon-gamma; interleukin-1 or interleukin-2; isoprinosine; Krestin; LC-9018; lamivudine; lentilart; LF-1695; methionine-enkephalin; [Minophagen] MINOPHAGEN® C (pharmaceutical preparations for the treatment of eczema, dermatitis, urticaria, and for the treatment of abnormal liver function resulting from chronic liver disease); muramyl tripeptide; naltrexone; nelfinavir; Neutropin; nevirapine; Nonoxinol; [Ornidyl] ORNIDYL® (eflornithine); non-nucleoside inhibitors of reverse transcriptase; nucleoside analogues (ddA, ddC, ddI, ddT, ddG, AZT, and the like); pentamidine isethionate; Phenytoin; polymannoacetate; Peptide T™ (octapeptide sequence); protease inhibitors;

Ribavirin; Rifabutin (ansamycin); ritonavir; RNA immunomodulator; rsT4 (recombinant soluble T4); saquinavir; shosaikoto and ginseng; SK-818 (germanium-derived antiviral); sodium diethylthiocarbamate; stavudine; stearic acid derivative; suramin and analogues thereof; thymic humoral factor; TP-5; Thymosin fraction 5 and Thymosin 1; Thymostimulin; TNF (tumor necrosis factor), vitamin B preparations; Trimetrexate; UA001;  $\alpha$ -interferon or acyclovir, for example.